

## WHAT IS CLAIMED IS:

1. A method of treating a plaque forming disease comprising the steps of:
  - (a) displaying a polypeptide on a display vehicle, said polypeptide representing at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said at least one epitope being capable of eliciting antibodies capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein; and
  - (b) introducing said display vehicle into a body of a recipient so as to elicit said antibodies capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein.
2. The method of claim 1, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.
3. The method of claim 1, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Straussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).
4. The method of claim 1, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.
5. The method of claim 1, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

6. The method of claim 5, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.
7. The method of claim 5, wherein said virus is a bacteriophage.
8. The method of claim 7, wherein said bacteriophage is a filamentous bacteriophage.
9. The method of claim 7, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.
10. The method of claim 7, wherein said bacteriophage is capable of propagation in *Escherichia coli*.
11. The method of claim 7, wherein said bacteriophage is fd.
12. The method of claim 1, wherein said display vehicle is an *in vivo* non-propagatable particle.
13. The method of claim 1, wherein said display vehicle is selected such that less than 30 days following an introduction of a triple dose of  $10^{10}$  units thereof to the recipient, a titer of said antibodies is above 1:50,000, as is determined by ELISA.
14. An agent for treating a plaque forming disease comprising a display vehicle displaying a polypeptide, said polypeptide representing at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said at least one epitope being capable of eliciting antibodies capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein.
15. The agent of claim 14, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late

onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

16. The agent of claim 14, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

17. The agent of claim 14, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

18. The agent of claim 14, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

19. The agent of claim 18, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

20. The agent of claim 18, wherein said virus is a bacteriophage.

21. The agent of claim 20, wherein said bacteriophage is a filamentous bacteriophage.

22. The agent of claim 20, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

23. The agent of claim 20, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

24. The agent of claim 20, wherein said bacteriophage is M13.

25. The agent of claim 14, wherein said display vehicle is an *in vivo* non-propagatable particle.

26. The agent of claim 14, wherein said display vehicle is selected such that less than 30 days following an introduction of a triple dose of  $10^{10}$  units thereof to the recipient, a titer of said antibodies is above 1:50,000, as is determined by ELISA.

27. A pharmaceutical composition for treating a plaque forming disease comprising an effective amount of a display vehicle displaying a polypeptide, said polypeptide representing at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said at least one epitope being capable of eliciting an effective amount of antibodies capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein, and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of claim 27, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

29. The pharmaceutical composition of claim 27, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

30. The pharmaceutical composition of claim 27, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

31. The pharmaceutical composition of claim 27, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

32. The pharmaceutical composition of claim 31, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

33. The pharmaceutical composition of claim 31, wherein said virus is a bacteriophage.

34. The pharmaceutical composition of claim 33, wherein said bacteriophage is a filamentous bacteriophage.

35. The pharmaceutical composition of claim 33, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

36. The pharmaceutical composition of claim 33, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

37. The pharmaceutical composition of claim 33, wherein said bacteriophage is fd.

38. The pharmaceutical composition of claim 27, wherein said display vehicle is an *in vivo* non-propagatable particle.

39. The pharmaceutical composition of claim 27, wherein said display vehicle is selected such that less than 30 days following an introduction of a triple dose of  $10^{10}$  units thereof to the recipient, a titer of said antibodies is above 1:50,000, as is determined by ELISA.

40. A method of preparing a display vehicle for treating a plaque forming disease, the method comprising the step of genetically modifying a genome of a display vehicle by inserting therein a polynucleotide sequence encoding a polypeptide representing at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said at least one epitope being capable of eliciting antibodies capable of

disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein, such that when said display vehicle propagates said polypeptide is displayed by said display vehicle.

41. The method of claim 40, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

42. The method of claim 40, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Straussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

43. The method of claim 40, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

44. The method of claim 40, wherein said display vehicle is selected from the group consisting of a virus and a bacteria.

45. The method of claim 45, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

46. The method of claim 47, wherein said virus is a bacteriophage.

47. The method of claim 46, wherein said bacteriophage is a filamentous bacteriophage.

48. The method of claim 46, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

49. The method of claim 46, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

50. The method of claim 46, wherein said bacteriophage is fd.

51. The method of claim 40, wherein said display vehicle is an *in vivo* non-propagatable particle.

52. The method of claim 40, wherein said display vehicle is selected such that less than 30 days following an introduction of a triple dose of  $10^{10}$  units thereof to the recipient, a titer of said antibodies is above 1:50,000, as is determined by ELISA.

53. A method of treating a plaque forming disease comprising the steps of:

- (a) displaying a polypeptide on a display vehicle, said polypeptide representing at least an immunological portion of an antibody being for binding at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said immunological portion of said antibody being capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein; and
- (b) introducing said display vehicle into a body of a recipient so as to disaggregate said aggregating protein.

54. The method of claim 53, wherein introducing said display vehicle into the body of the recipient so as to disaggregate said aggregating protein is by applying said display vehicle to an olfactory system of the recipient.

55. The method of claim 53, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late

onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

56. The method of claim 53, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Straussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

57. The method of claim 53, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

58. The method of claim 53, wherein said at least one epitope of said prion protein is defined by at least a portion of an amino acid sequence set forth in SEQ ID NO:25.

59. The method of claim 53, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

60. The method of claim 59, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

61. The method of claim 59, wherein said virus is a bacteriophage.

62. The method of claim 61, wherein said bacteriophage is a filamentous bacteriophage.

63. The method of claim 61, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.



64. The method of claim 61, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

65. The method of claim 61, wherein said bacteriophage is fd.

66. The method of claim 53, wherein said display vehicle is an *in vivo* non-propagatable particle.

67. An agent for treating a plaque forming disease comprising a display vehicle displaying a polypeptide representing at least an immunological portion of an antibody being for binding at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said immunological portion of said antibody being capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein.

68. The agent of claim 67, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

69. The agent of claim 67, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

70. The agent of claim 69, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

71. The agent of claim 69, wherein said at least one epitope of said prion protein is formed by an amino acid sequence set forth in SEQ ID NO:25.

72. The agent of claim 69, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

73. The agent of claim 72, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

74. The agent of claim 72, wherein said virus is a bacteriophage.

75. The agent of claim 74, wherein said bacteriophage is a filamentous bacteriophage.

76. The agent of claim 74, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

77. The agent of claim 74, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

78. The agent of claim 74 wherein said bacteriophage is fd.

79. The agent of claim 67, wherein said display vehicle is an *in vivo* non-propagatable particle.

80. A pharmaceutical composition for treating a plaque forming disease comprising an effective amount of a display vehicle displaying a polypeptide representing at least an immunological portion of an antibody being for binding at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said immunological portion of said antibody being capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein, the pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

81. The pharmaceutical composition of claim 80, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

82. The pharmaceutical composition of claim 80, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

83. The pharmaceutical composition of claim 80, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

84. The pharmaceutical composition of claim 80, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

85. The pharmaceutical composition of claim 84, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

86. The pharmaceutical composition of claim 84, wherein said virus is a bacteriophage.

87. The pharmaceutical composition of claim 86, wherein said bacteriophage is a filamentous bacteriophage.

88. The pharmaceutical composition of claim 86, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

89. The pharmaceutical composition of claim 86, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

90. The pharmaceutical composition of claim 84, wherein said bacteriophage is fd.

91. The pharmaceutical composition of claim 80, wherein said display vehicle is an *in vivo* non-propagatable particle.

92. A method of preparing a display vehicle for treating a plaque forming disease, the method comprising the step of genetically modifying a genome of a display vehicle by inserting therein a polynucleotide sequence encoding at least an immunological portion of an antibody being for binding at least one epitope of an aggregating protein associated with plaque formation in said plaque forming disease, said immunological portion of said antibody being capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein.

93. The method of claim 92, wherein the plaque forming disease is selected from the group consisting of early onset Alzheimer's disease, late onset Alzheimer's disease, presymptomatic Alzheimer's disease, SAA amyloidosis, hereditary Icelandic syndrome, senility and multiple myeloma.

94. The method of claim 92, wherein the plaque forming disease is selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

95. The method of claim 92, wherein said aggregating protein is selected from the group consisting of beta-amyloid, serum amyloid A, cystatin C, IgG kappa light chain and prion protein.

96. The method of claim 92, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

97. The method of claim 96, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

98. The method of claim 96, wherein said virus is a bacteriophage.

99. The method of claim 98, wherein said bacteriophage is a filamentous bacteriophage.

100. The method of claim 98, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

101. The method of claim 98, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

102. The method of claim 98, wherein said bacteriophage is fd.

103. The method of claim 92, wherein said display vehicle is an *in vivo* non-propagatable particle.

104. A method of introducing a display vehicle lacking an engineered targeting moiety into a brain of a recipient, the method comprising the step of administering said display vehicle intranasally to the recipient.

105. The method of claim 104, wherein said display vehicle is selected from the group consisting of a virus, a bacteria and a polypeptide carrier.

106. The method of claim 105, wherein said virus is selected from the group consisting of a double stranded DNA virus, a single stranded DNA virus, a positive strand RNA virus and a negative strand RNA virus.

107. The method of claim 105, wherein said virus is a bacteriophage.

108. The method of claim 107, wherein said bacteriophage is a filamentous bacteriophage.

109. The method of claim 107, wherein said bacteriophage is capable of propagation in bacterial flora in said recipient.

110. The method of claim 107, wherein said bacteriophage is capable of propagation in *Escherichia coli*.

111. The method of claim 107, wherein said bacteriophage is fd.

112. The method of claim 104, wherein said display vehicle is an *in vivo* non-propagatable particle.

113. The method of claim 104, wherein the display vehicle displays at least an immunological portion of an antibody.

114. The method of claim 104, wherein said immunological portion of an antibody serves for binding at least one epitope of an aggregating protein associated with plaque formation in a plaque forming disease, said immunological portion of said antibody being capable of disaggregating said aggregating protein and/or of preventing aggregation of said aggregating protein.

115. A polypeptide comprising at least an immunological portion of an antibody being capable disaggregating a prion protein aggregate and/or of preventing aggregation of said prion protein.

116. The polypeptide of claim 115, wherein the polypeptide is capable of binding at least one epitope formed by an amino acid sequence set forth in SEQ ID NO:25.

117. The polypeptide of claim 116, wherein said prion protein is a scrapie isoform (PrP<sup>sc</sup>) associated with the formation of a plaque forming disease selected from the group consisting of scrapie, bovine spongiform encephalopathy (BSE), kuru, Creutzfeldt-Jakob Disease (CJD), Gerstmann-Streussler-Sheinker Disease (GSS) and fatal familial insomnia (FFI).

118. A method of detecting a presence or an absence of a prion protein in a biological sample, the method comprising the steps of:

- (a) incubating an anti-prion antibody or an immunological portion thereof with the biological sample; and
- (b) determining a presence or an absence of antigen complexes formed with said anti-prion antibody or said immunological portion thereof, to thereby determine the presence or the absence of the prion protein in the biological sample.

119. The method of claim 118, wherein the prion protein is an aggregating protein associated with plaque formation.

120. The method of claim 118, wherein said anti-prion antibody or said immunological portion thereof is directed against at least one epitope formed by an amino acid sequence set forth in SEQ ID NO:25.

121. The method of claim 118, wherein the biological sample is derived from tissues or body fluids of a mammal selected from the group consisting of a human, a primate, a monkey, a pig, a bovine, a sheep, a deer, an elk, a cat and a dog.